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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| CRANE, LAWRENCE E | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | |

DATE MAILED: 04/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/756,411 | LORI ET AL. | |
| | Examiner | Art Unit | |
| | L. E. Crane | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *21-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

No claims have been cancelled, no claims have been amended, the disclosure has not been amended, and no new claims have been added as per the response filed December 20, 2004. No additional Information Disclosure Statements or other declarations have been filed as of the date of this Office action.

Claims **21-30** remain in the case.

Claims **21-30** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims **21-30** are directed to pairs of compounds, the specific chemical identities of which either have not been specified or have been only specified in part, and are therefore claimed more broadly than is supportable by the instant disclosed exemplification.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant argues that the written description requirement has been met by the Vila declaration. Examiner respectfully disagrees. Referring to the Vila declaration applicant argues that Vila's assertion, "[in view of the efficacy of] the combination of hydroxyurea ... and ddI, a nucleoside reverse transcriptase inhibitor (NRTI), it is obvious that this principle should be viable for the combination of [hydroxyurea and other ribonucleotide reductase inhibitors with] other NRTI's" is adequate to permit the functional language noted above to be relied upon in a patent claim. Examiner takes a different view, noting that the included term "should be viable" is a clear indication that Vila is speculating. Examiner is also of the view that the Vila argument is directed to enablement, not written description.

Applicant argues in addition that "[t]he phrases 'an inhibitor of ribonucleotide reductase' and 'an antiviral nucleoside phosphate analog' are as accurate as the subject matter permits, such components of a mixture being undefinable by 'chicken wire' structural formulas." Examiner respectfully disagrees, noting that the application of generic chemical (chicken wire) structures and associated disclosures wherein the compound(s) contemplated to be included

within the scope of an invention directed to oligonucleotide and/or nucleoside/nucleotide pharmaceuticals has long been solved as anyone familiar with the body of patents included now found within Class 51, subclasses 42-51. The fundamental problems being debated here are a consequence of a specification which fails to include a sufficiently detailed description, meaning that there is a wide gap between the specifically described embodiments (described by specific "chicken wire" formulas) and the quoted generic terms at issue. Examiner does not think that this gap can be bridged by additional data. But, as also noted in the response following the enablement rejection, any additional data would be welcome and would permit claims more broadly defined that the claims in Malley et al. '161 (PTO-892 ref. **E**), but in no event as broadly defined as the independent claims presently at issue here.

Applicant argues further that "[t]he Patent Office maintained it rejection of the claims despite the Declaration of Dr. Vila." Examiner respectfully disagrees. The rejection has been maintained because applicant is claiming more subject matter than can be justified by the disclosure and the declarations in light of the applicable statutes and cited references.

Applicant then argues at page 6 of the response that "[f]actual evidence, however, must be accepted by the PTO." Examiner agrees and has again reviewed the Palmer and Sumpter references (PTO-892 refs. **WC** and **VC**, respectively) and finds the disclosures relevant, but not helpful. Applicant made an advance in HIV treatment but failed to carry forth the research and the associated CIP applications required to establish and/or extend the metes and bounds of the invention. Applicant is reminded that *Brenner v. Manson,* 148 USPQ 689 (S. Ct., 1966) is still applicable and at p. 696, column 1, stands for the proposition that "[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful completion." As Sumpter discloses repeatedly citing many sources, and as the apparent failure of the Phase III Trials of the HU/ddI as an HIV treatment appears to confirm, the treatment of HIV with HU (hydroxyurea) and ddI has well known risks including inhibition of bone marrow activity by HU, the likely reason for the rumored Phase III failure. Therefore, examiner concludes that while applicant's initial finding disclosed in Malley et al. '161 was a breakthrough, applicant's data of record is insufficient to establish that applicant had reason to know at the time of filing or subsequently that the claimed method of treating was generic in any sense, let alone to the degree claimed. The Palmer and Sumpter references establish only that applicant's appear to have guessed correctly, not that applicant has supported the written description generically by citing their results; e.g. examiner has not found within the instant

disclosure formulas or chemical names defining or describing the structural limitations which predict the activities of the particular carboxamic acid and hydroxamic acid disclosed by Sumpter to be effective replacements for hydroxyurea. As in *Ex parte Balzarini,* a written description of guesses about the possible scope of pharmacological activity are not an acceptable supporting basis in the absence of medicinally appropriate data in support thereof. As noted previously, applicant's own disclosure fails to provide the requisite support.

For these reasons, applicant's assertions have been considered but have not been found sufficient to overcome the instant grounds of rejection.

Claims **21-30** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims is difficult to determine because of reliance on functional terminology in claim **21** including the terms "an inhibitor of ribonucleotide reductase" and "an antiviral nucleoside phosphate analog."

B. The nature of the invention is limited to the inhibition of replication of a reverse transcriptase dependent virus in any host from a single cell to a complete human host. This encompasses the treatment of HIV in a human host.

C. The state of the prior art is well defined by the extensive list of prior art references in the PTO-892 and PTO-1449 of record. However, the prior art most relevant to the instant claims is limited to the patent and non-patent references from Mssrs. Malley and Vila (US 5,521,161 etc.) wherein the only operative embodiment supporting the instant claims is disclosed.

D. The level of one or ordinary skill is low because only a single prior art exemplification is known in the art.

E. The level of predictability in the art is low because of the existence of only a single enabling prior art exemplification (hydroxyurea/ddI) is known in the prior art.

F. The amount of direction provided by the inventor is, with the exception of the known exemplification, all prospective and therefore not useful in determining whether the prior art exemplification is a singular observation or whether analogous phenomena occur with other combinations of active ingredients.

G. The existence of working examples is limited to the single prior art exemplification, the remaining examples all being prospective; i.e. experimentally unsupported.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because of the absence of working examples to provide a proper basis for extrapolation to other combinations of active ingredients. See also *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991) which in its first opinion stands for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment (MPEP at 2107.03 (p. 2100-44, col. 2, in the August, 2001 revision)).

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant is advised that examiner has heard rumors from three informed sources that the Phase III (FDA type) Trial of the Malley/Vila method of HIV treatment (hydroxyurea + ddI as disclosed in US 5,521,161) was determined to have <u>failed</u> because a single mortality was observed, and that this result meant that this technology was considered a failure and would not be further pursued. Furthermore, the rumor attributes the death to side effect(s) of ddI, as suggested by a similar circumstance disclosed in **Parker et al.** (PTO-892 ref. **XC**) and supported by several reports of the potentially lethal side effects of hydroxyurea noted in **Sumpter et al**. Examiner is only capable of speculating on this result, and because of the

confidential nature of the Phase III Trial results, has not been able confirm in a published report the reason(s) for this failure. Therefore, examiner respectfully requests any and all reports on this test which are known to applicant so same can be made of record in the instant case.

Applicant argues that the instant claims are allowable in light of the guidance of *Ex parte Balzarini* and further argues that the declaration of inventor Vila "... must be accepted by the PTO" in light of the guidance of *In re Brana*. Examiner respectfully disagrees. Applicant is free to submit declarations and the PTO is required to consider same, but is not required to accept the arguments provided therein as anything but the informed opinion of the declarant. Said opinions may or may not be found to be convincing.

Claims **21-30** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims **21-30** one or both of the active ingredients have not been specified with other than with functional language, and therefore each noted claim lacks properly defined metes and bounds because the ordinary practitioner cannot determine what is included or excluded, or what was included or excluded at the time of filing.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant argues that the above rejection has found the instant claims to be "omnibus claims" as defined in the MPEP at §2173.05(r). Examiner respectfully disagrees. The above rejection points out that functional language of the kind noted causes failure of the claims containing same to have adequately defined metes and bounds. Applicant has failed to respond to the rejection as stated above.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d

937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-28** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***12-22*** of U.S. Patent No. **6,046,175** (PTO-892 ref. **H**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-27 and 29-30** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***3-8*** of U.S. Patent No. **6,194,390** (PTO-892 ref. **J**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a

human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-28** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-3*** of U.S. Patent No. **5,521,161** (PTO-892 ref. **E**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-28** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-3*** of U.S. Patent No. **5,736,527** (PTO-892 ref. **G**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a method of treating HIV in a human host wherein the active ingredients are defined generically in a manner which includes the subject matter of the previously patented claims.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-28** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims ***6-8*** of U.S. Patent No. **6,093,702** (PTO-892 ref. **K**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to a binary composition which includes two active ingredients generically defined in a manner which includes the subject matter previously claimed.

Applicant's arguments and responses filed December 20, 2004 have been fully considered but they are not persuasive.

Applicant has acknowledged the possible appropriateness of the instant rejection has not provided an appropriate terminal disclaimer.

Claims **21-30** would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. §112 and if the appropriate terminal disclaimers have been entered.

**THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 703-872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached at **571-272-0661**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
**03/31/2005**

Thomas C. McKenzie, Ph.D.
Primary Patent Examiner
Technology Center 1600